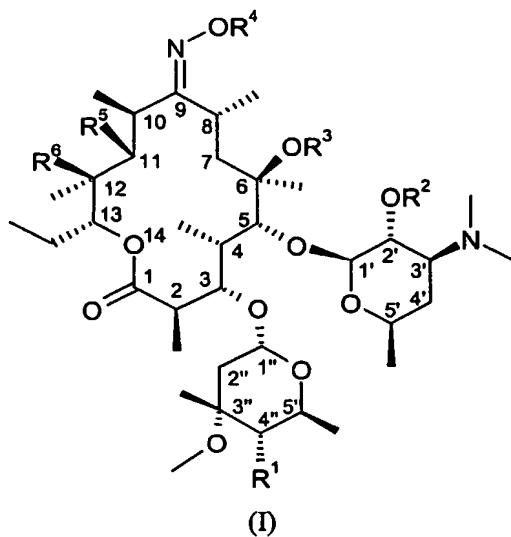
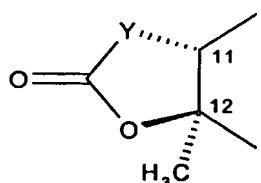


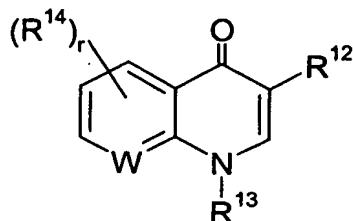
Claims

## 1. A compound of general formula (I)

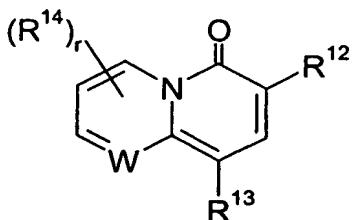


wherein

R<sup>1</sup> is OC(O)(CH<sub>2</sub>)<sub>m</sub>XR<sup>7</sup>;R<sup>2</sup> is hydrogen or a hydroxyl protecting group;10 R<sup>3</sup> is hydrogen, C<sub>1-4</sub>alkyl or C<sub>3-6</sub>alkenyl optionally substituted by 9 to 10 membered fused bicyclic heteroaryl;R<sup>4</sup> is hydrogen, C<sub>1-4</sub>alkyl, C<sub>3-7</sub>cycloalkyl, C<sub>3-6</sub>alkenyl or a 5 or 6 membered heterocyclic group, wherein the alkyl, cycloalkyl, alkenyl and heterocyclic groups are optionally substituted by up to three substituents independently selected from optionally substituted 5 or15 6 membered heterocyclic group, optionally substituted 5 or 6 membered heteroaryl, OR<sup>8</sup>, S(O)<sub>n</sub>R<sup>8</sup>, NR<sup>8</sup>R<sup>9</sup>, CONR<sup>8</sup>R<sup>9</sup>, halogen and cyano;R<sup>5</sup> is hydroxy, C<sub>3-6</sub>alkenyoxy optionally substituted by 9 to 10 membered fused bicyclic heteroaryl, or O(CH<sub>2</sub>)<sub>p</sub>O(CH<sub>2</sub>)<sub>q</sub>R<sup>10</sup>,R<sup>6</sup> is hydroxy, or20 R<sup>5</sup> and R<sup>6</sup> taken together with the intervening atoms form a cyclic group having the following structure:wherein Y is a bivalent radical selected from -CH<sub>2</sub>- , -CH(CN)-, -O-, -N(R<sup>11</sup>)- and -CH(SR<sup>11</sup>)-;25 R<sup>7</sup> is a heterocyclic group having the following structure:



or



R<sup>8</sup> and R<sup>9</sup> are each independently selected from hydrogen and C<sub>1</sub>-4alkyl;

5 R<sup>10</sup> is hydrogen or NR<sup>8</sup>R<sup>9</sup>;

R<sup>11</sup> is hydrogen or C<sub>1</sub>-4alkyl substituted by a group selected from optionally substituted phenyl, optionally substituted 5 or 6 membered heteroaryl and optionally substituted 9 to 10 membered fused bicyclic heteroaryl;

R<sup>12</sup> is hydrogen, C(O)OR<sup>15</sup>, C(O)NHR<sup>15</sup> or C(O)CH<sub>2</sub>NO<sub>2</sub>;

10 R<sup>13</sup> is hydrogen, C<sub>1</sub>-4alkyl optionally substituted by hydroxy or C<sub>1</sub>-4alkoxy, C<sub>3</sub>-7cycloalkyl, or optionally substituted phenyl or benzyl;

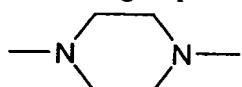
R<sup>14</sup> is halogen, C<sub>1</sub>-4alkyl, C<sub>1</sub>-4thioalkyl, C<sub>1</sub>-4alkoxy, NH<sub>2</sub>, NH(C<sub>1</sub>-4alkyl) or N(C<sub>1</sub>-4alkyl)<sub>2</sub>;

R<sup>15</sup> is hydrogen or C<sub>1</sub>-4alkyl optionally substituted by up to three groups independently selected from halogen, C<sub>1</sub>-4alkoxy, OC(O)C<sub>1</sub>-4alkyl and OC(O)OC<sub>1</sub>-4alkyl;

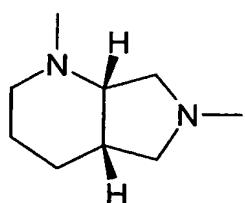
R<sup>16</sup> is hydrogen, C<sub>1</sub>-4alkyl, C<sub>3</sub>-7cycloalkyl, optionally substituted phenyl or benzyl, acetyl or benzoyl;

R<sup>17</sup> is hydrogen or R<sup>14</sup>, or R<sup>17</sup> and R<sup>13</sup> are linked to form the bivalent radical -O(CH<sub>2</sub>)<sub>2</sub>- or -(CH<sub>2</sub>)<sub>v</sub>-;

20 X is -U(CH<sub>2</sub>)<sub>s</sub>Z- or X is a group selected from:



and



25 U and Z independently are a divalent radical selected from -N(R<sup>16</sup>)-, -O-, -S(O)<sub>t</sub>-, -N(R<sup>16</sup>)C(O)-, -C(O)N(R<sup>16</sup>)- and -N[C(O)R<sup>16</sup>]-;

W is CR<sup>17</sup> or a nitrogen atom;

m is 0 or an integer from 1 to 5;

n, r and t are each independently selected from 0, 1 and 2;  
 p and q are each independently selected from 1 to 6;  
 s is an integer from 2 to 8; and  
 v is 2 or 3;

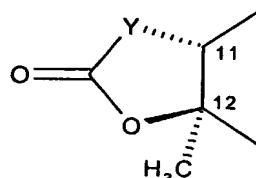
5 and pharmaceutically acceptable derivatives thereof.

2. A compound according to claim 1 wherein R<sup>2</sup> is hydrogen.

3. A compound according to claim 1 or 2 wherein R<sup>3</sup> is hydrogen.

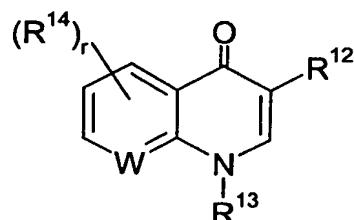
10 4. A compound according to any one of the preceding claims wherein R<sup>4</sup> is hydrogen or C<sub>1-4</sub>alkyl optionally substituted by up to three substituents independently selected from optionally substituted 5 or 6 membered heteroaryl, OR<sup>8</sup>, S(O)<sub>n</sub>R<sup>8</sup>, NR<sup>8</sup>R<sup>9</sup>, halogen and cyano.

15 5. A compound according to any one of the preceding claims wherein R<sup>5</sup> is hydroxy or O(CH<sub>2</sub>)<sub>p</sub>O(CH<sub>2</sub>)<sub>q</sub>R<sup>10</sup> and R<sup>6</sup> is hydroxy, or R<sup>5</sup> and R<sup>6</sup> taken together with the intervening atoms form a cyclic group having the following structure:



20 wherein Y is the bivalent radical -O-.

6. A compound according to any one of the preceding claims wherein R<sup>7</sup> is a heterocyclic group having the following structure:



25 wherein W is CR<sup>17</sup> where R<sup>17</sup> is hydrogen.

7. A compound according to any one of the preceding claims wherein X is -U(CH<sub>2</sub>)<sub>s</sub>Z- wherein U and Z are independently -NH- or -O-.

30 8. A compound according to claim 1 as defined in any one of Examples 1 to 15, or a pharmaceutically derivative thereof.

9. A compound selected from:

4"-*O*-[3-[[2-[(3-carboxy-7-chloro-1-cyclopropyl-1,4-dihydro-4-oxo-6-quinolinyl) amino]ethyl]amino]propionyl]-11-*O*-(2-dimethylaminoethoxymethyl)-(9E)-methoximino erythromycin A,

4"-*O*-[3-[[2-[(3-carboxy-7-chloro-1-cyclopropyl-1,4-dihydro-4-oxo-6-quinolinyl) amino]ethyl]amino]propionyl]-11,12-carbonate-(9E)-*O*-(2-propyl)oximino erythromycin A,

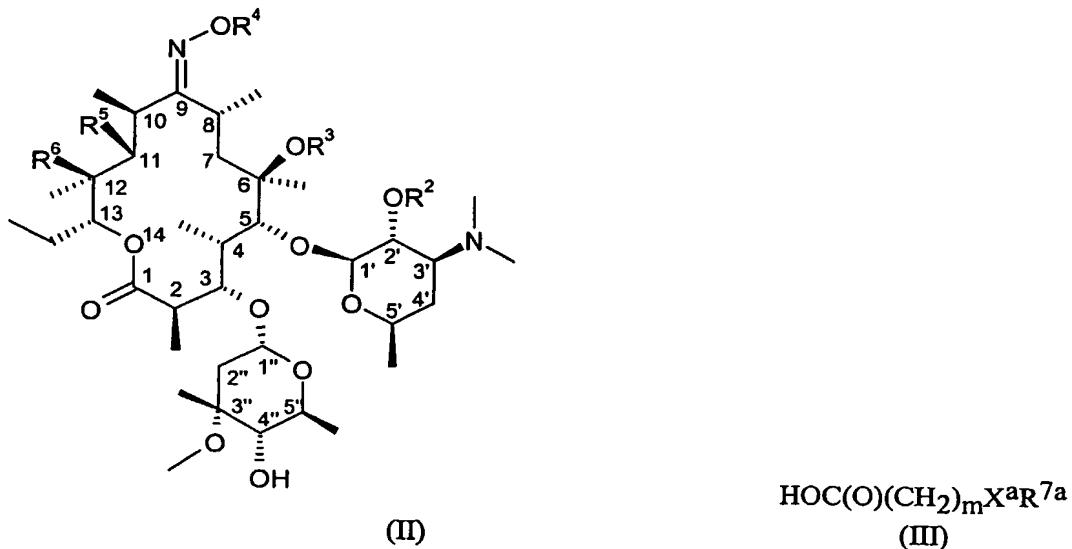
4"-*O*-[3-[[2-[(3-carboxy-7-chloro-1-cyclopropyl-1,4-dihydro-4-oxo-6-quinolinyl) amino]ethyl]amino]propionyl]-11,12-carbonate-(9E)-methoximino erythromycin A, and

10 4"-*O*-[3-[[2-[(3-carboxy-7-chloro-1-cyclopropyl-1,4-dihydro-4-oxo-6-quinolinyl) amino]ethyl]amino]propionyl]-11,12-carbonate-(9E)-*O*-(ethoxymethyl)oximino erythromycin A,

or a pharmaceutically acceptable derivative thereof.

15 10. A process for the preparation of a compound as claimed in claim 1 which comprises:

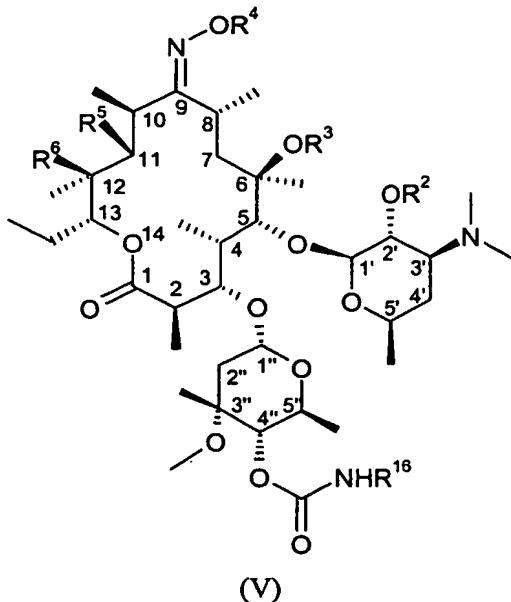
a) reacting a compound of formula (II)



20 with a suitable activated derivative of the acid (III), wherein m is an integer 1 to 5, X<sup>a</sup> and R<sup>7a</sup> are X and R<sup>7</sup> as defined in claim 1 or groups convertible to X and R<sup>7</sup>, to produce a compound of formula (I) wherein m is an integer 1 to 5;

25 b) reacting a compound of formula (II), in which the 4" hydroxy is suitably activated, with a compound of formula X<sup>a</sup>R<sup>7a</sup> (IV), wherein R<sup>7a</sup> is R<sup>7a</sup> as defined in claim 1 or a group convertible to R<sup>7</sup>, s and Z have the meanings defined in claim 1 and X<sup>a</sup> is -U(CH<sub>2</sub>)<sub>s</sub>Z- or a group convertible to -U(CH<sub>2</sub>)<sub>s</sub>Z-, in which U is a group selected from selected from -N(R<sup>16</sup>)-, -O-, and -S-, to produce a compound of formula (I) wherein m is 0 and U is a group selected from -N(R<sup>16</sup>)-, -O- and -S-;

30 c) reacting a compound of formula (V)

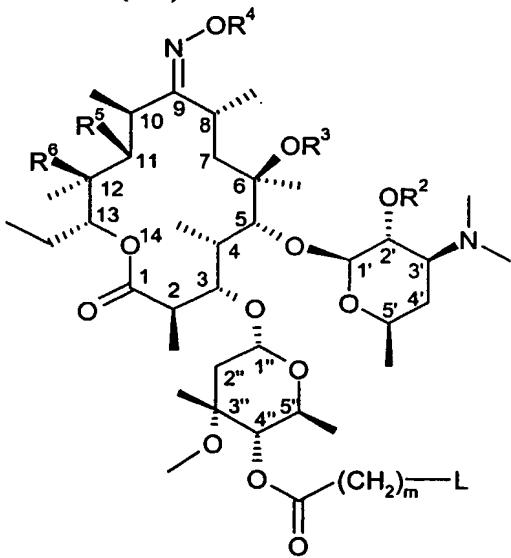


(V)

wherein  $R^{16}$  has the meaning defined in claim 1 with a suitable activated derivative of the carboxylic acid  $HOC(O)(CH_2)_sZ^aR^{7a}$  (VI), wherein  $R^{7a}$  and  $Z^a$  are  $R^7$  and  $Z$  as defined in claim 1 or groups convertible to  $R^7$  and  $Z$ , to produce a compound of formula (I) wherein  $m$  is 0 and  $U$  is  $-N(R^{16})C(O)-$ ;

5 d) reacting a compound of formula (II) with a suitably activated derivative of the carboxylic acid  $HOC(O)C(O)N(R^{16})(CH_2)_sZ^aR^{7a}$  (VIIb) to produce a compound of formula (I) wherein  $m$  is 0 and  $U$  is  $-C(O)N(R^{16})-$ ;

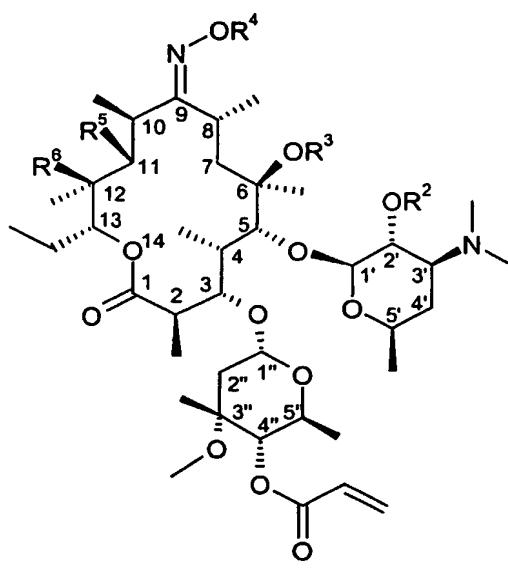
10 e) reacting a compound of formula (VII)



(VII)

15 with a compound of formula  $X^aR^{7a}$  (IV), wherein  $R^{7a}$  and  $X^a$  are  $R^7$  and  $X$  as defined in claim 1 or groups convertible to  $R^7$  and  $X$ ,  $U$  is a group selected from  $-N(R^{16})-$ ,  $-O-$  and  $-S-$ , and  $L$  is suitable leaving group, to produce a compound of formula (I) wherein  $m$  is 1 to 5 and  $U$  is a group selected from  $-N(R^{16})-$ ,  $-O-$  and  $-S-$ ; or

f) reacting a compound of formula (IX), with a compound of formula  $X^aR^{7a}$  (IV),



5

(IX)

wherein  $R^{7a}$  and  $X^a$  are  $R^7$  and  $X$  as defined in claim 1 or groups convertible to  $R^7$  and  $X$ ,  $U$  is a group selected from  $-N(R^{16})-$ ,  $-O-$  and  $-S-$ , to produce a compound of formula (I) wherein  $m$  is 2 and  $U$  is a group selected from  $-N(R^{16})-$ ,  $-O-$  and  $-S-$ ;

10

and thereafter, if required, subjecting the resulting compound to one or more of the following operations:

- i) removal of the protecting group  $R^2$ ,
- ii) conversion of  $X^aR^{7a}$  or  $Z^aR^{7a}$  to  $XR^7$  or  $ZR^7$  respectively, and

15     iii) conversion of the resultant compound of formula (I) into a pharmaceutically acceptable derivative thereof.

11.     A compound as claimed in any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof for use in therapy.

20

12.     The use of a compound as claimed in any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof in the preparation of a medicament for use in the therapy of systemic or topical microbial infections in a human or animal body.

25

13.     The use of a compound as claimed in any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof for use in the treatment or prophylaxis of systemic or topical microbial infections in a human or animal body.

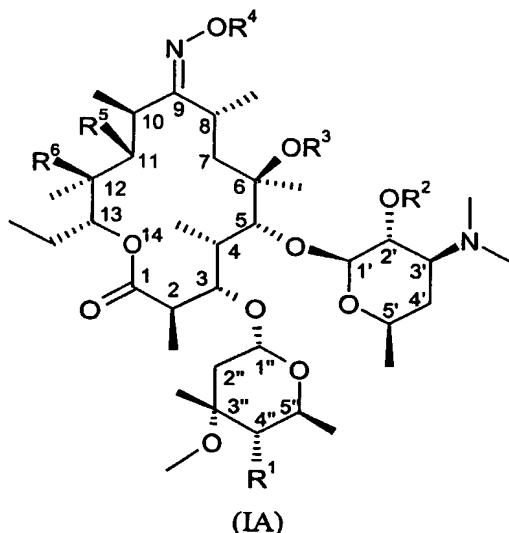
30

14.     A pharmaceutical composition comprising a compound as claimed any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof in admixture with one or more pharmaceutically acceptable carriers or excipients.

15. A method for the treatment of the human or non-human animal body to combat microbial infection comprising administration of an effective amount of a compound as claimed in any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof.

5

16. A compound of general formula (IA)



10 wherein

R<sup>1</sup> is OC(O)(CH<sub>2</sub>)<sub>m</sub>XR<sup>7</sup>;

R<sup>2</sup> is hydrogen or a hydroxyl protecting group;

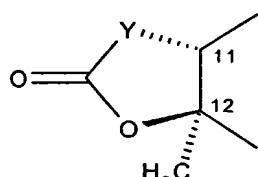
R<sup>3</sup> is hydrogen, C<sub>1-4</sub>alkyl or C<sub>3-6</sub>alkenyl optionally substituted by 9 to 10 membered fused bicyclic heteroaryl;

15 R<sup>4</sup> is hydrogen, C<sub>1-4</sub>alkyl, C<sub>3-7</sub>cycloalkyl, C<sub>3-6</sub>alkenyl or a 5 or 6 membered heterocyclic group, wherein the alkyl, cycloalkyl, alkenyl and heterocyclic groups are optionally substituted by up to three substituents independently selected from optionally substituted 5 or 6 membered heterocyclic group, optionally substituted 5 or 6 membered heteroaryl, OR<sup>8</sup>, S(O)<sub>n</sub>R<sup>8</sup>, NR<sup>8</sup>R<sup>9</sup>, CONR<sup>8</sup>R<sup>9</sup>, halogen and cyano;

20 R<sup>5</sup> is hydroxy, C<sub>3-6</sub>alkenyoxy optionally substituted by 9 to 10 membered fused bicyclic heteroaryl or O(CH<sub>2</sub>)<sub>p</sub>O(CH<sub>2</sub>)<sub>q</sub>R<sup>10</sup>,

R<sup>6</sup> is hydroxy, or

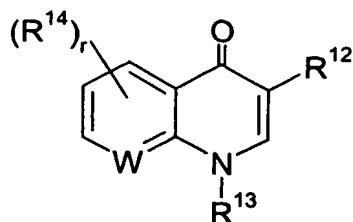
R<sup>5</sup> and R<sup>6</sup> taken together with the intervening atoms form a cyclic group having the following structure:



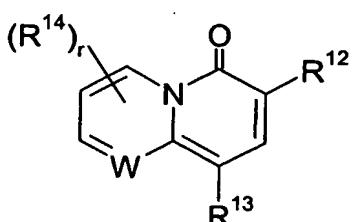
25

wherein Y is a bivalent radical selected from -CH<sub>2</sub>-, -CH(CN)-, -O-, -N(R<sup>11</sup>)- and -CH(SR<sub>8</sub>)-;

R<sup>7</sup> is a heterocyclic group having the following structure:



or



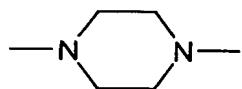
5 R<sup>8</sup> and R<sup>9</sup> are each independently selected from hydrogen and C<sub>1</sub>-4alkyl;  
 R<sup>10</sup> is hydrogen or NR<sup>8</sup>R<sup>9</sup>;

R<sup>11</sup> is hydrogen or C<sub>1</sub>-4alkyl substituted by a group selected from optionally substituted phenyl, optionally substituted 5 or 6 membered heteroaryl and optionally substituted 9 to 10 membered fused bicyclic heteroaryl;

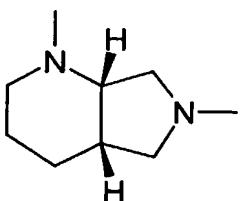
10 R<sup>12</sup> is hydrogen, C(O)OR<sup>15</sup>, C(O)NHR<sup>15</sup> or C(O)CH<sub>2</sub>NO<sub>2</sub>;  
 R<sup>13</sup> is hydrogen, C<sub>1</sub>-4alkyl, C<sub>3</sub>-7cycloalkyl, or optionally substituted phenyl or benzyl;  
 R<sup>14</sup> is halogen, C<sub>1</sub>-4alkyl, C<sub>1</sub>-4thioalkyl, C<sub>1</sub>-4alkoxy, NH<sub>2</sub>, NH(C<sub>1</sub>-4alkyl) or N(C<sub>1</sub>-4alkyl)<sub>2</sub>;  
 R<sup>15</sup> is hydrogen or C<sub>1</sub>-4alkyl;

15 R<sup>16</sup> is hydrogen, C<sub>1</sub>-4alkyl, C<sub>3</sub>-7cycloalkyl, optionally substituted phenyl or benzyl, acetyl or benzoyl;

X is -U(CH<sub>2</sub>)<sub>s</sub>Z- or X is a group selected from:



and



20

U and Z independently are a divalent radical selected from -N(R<sup>16</sup>)-, -O-, -S(O)<sub>t</sub>-, N(R<sup>16</sup>)C(O)-, -C(O)N(R<sup>16</sup>)- and -N[C(O)R<sup>16</sup>]-;

W is a carbon or a nitrogen atom;

25 m is 0 or an integer from 1 to 5;

n, r and t are each independently selected from 0, 1 and 2;

p and q are each independently selected from 1 and 2; and

s is an integer from 2 to 8;

and pharmaceutically acceptable salts and solvates thereof.